Deciphering the molecular mechanism of signal transducing adaptor family member (STAP) 1 in the regulation of hepatic lipid metabolism

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Introduction

The prevalence of non-alcoholic fatty liver disease (NAFLD) is growing in both developed and developing countries in the past decades. Additionally, increasing clinical evidences suggest that NAFLD can not only confined as liver-related morbidity and mortality, but is a multisystem disease that affecting whole body metabolism and participating in the onset of type 2 diabetes (T2D), obesity, cardiovascular (CDV) and cardiac diseases. However, there is no regulatory approved drug for NAFLD up to date. Thus, it is urgent to investigate new therapies for NAFLD. Signal transducing adaptor family member 1 (STAP1) is a novel gene which has been considered to cause familial hypercholesterolemia (FH) due to the mutations. Other reports suggest there is no correlation between the mutations of STAP1 and blood lipids levels. Despite the controversial findings in the clinical studies, a dramatic increase of the expression levels of STAP1 was found in the liver of our NAFLD mice. Thus, this study aims to investigate the role of STAP1 in the development of NAFLD.

Methodology

C57BL/6N wildtype (WT) mice were fed with high-fat diet (HFD) for 12 weeks to develop diet-induced obesity (DIO) for NAFLD model. Liver, epididymal white adipose tissue (eWAT) and skeletal muscle were collected for quantitative real-time polymerase chain reaction (qPCR) analyses. Liver tissues were also used for liver fractionation. Flow cytometry was used to measure the cell composition within liver and adipose tissue upon standard chow diet (STC) and HFD feeding.

Results

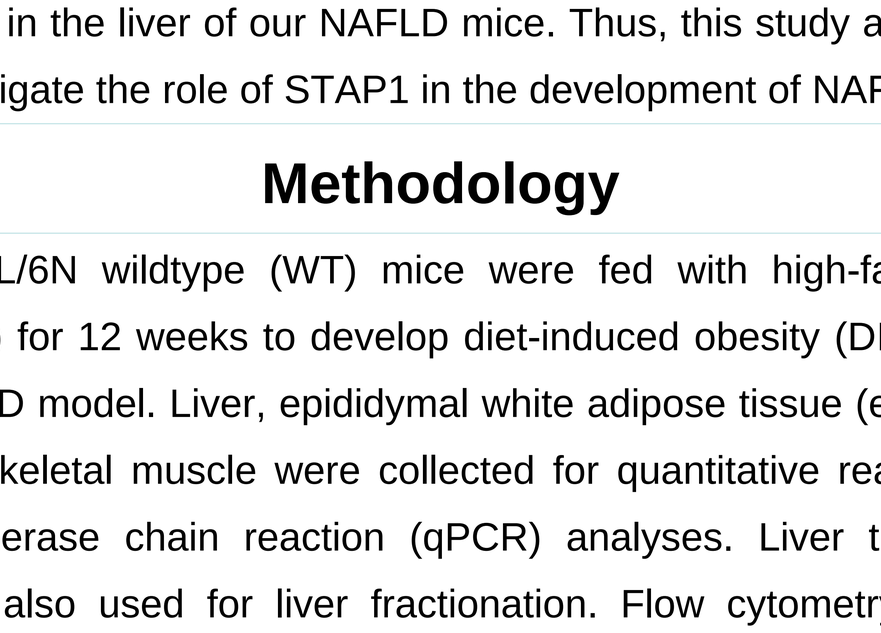

Figure 1. STAP1 was significantly and specifically induced in livers of obese mice. 8-week-old male C57BL/6N WT or STAP1 KO mice were fed with 45% high-fat diet (HFD) for 3 months. mRNA expression levels of STAP1 in liver, spleen, epididymal adipose tissue (VAT) and muscle were measured by using qPCR analysis. N=4, $^{**}P < 0.01$.

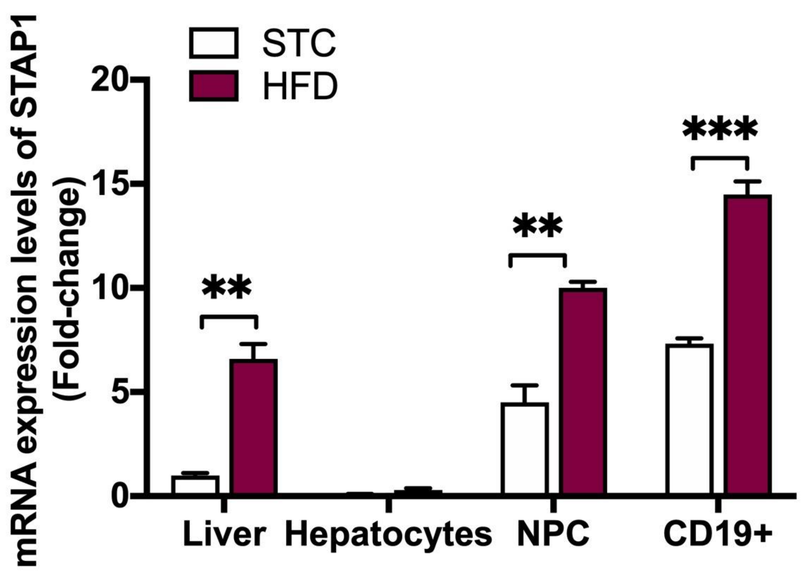

Figure 2. STAP1 was significantly induced in the intrahepatic B cells of obese mice. 8-week-old male C57BL/6N WT or STAP1 KO mice were fed with 45% high-fat diet (HFD) for 3 months. mRNA expression levels of STAP1 in different liver fractions and CD19 positive cells were measured by using qPCR analysis. N=4, $^{**}P < 0.01$ and $^{***}P < 0.001$. (NPC, non-parenchymal cells.)

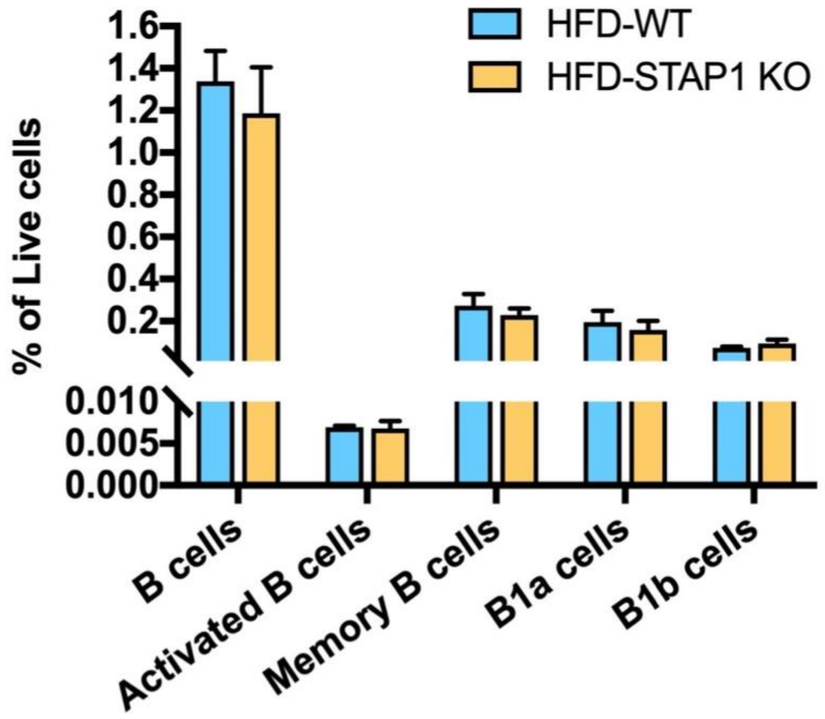

Figure 3. The population of subsets of intrahepatic B cells in STAP1 depletion obese mice remains no changes. 8-week-old male C57BL/6N WT or STAP1 KO mice were fed with 45% high-fat diet (HFD) for 3 months. Non-parenchymal cells (NPC) were isolated for flow cytometry analysis. N=4. (B cells, CD19+ CD45R+; Activated B cells, CD19+ CD45R+ CD40+ CD86-; Memory B cells, CD19+ CD45R+ CD40+ CD86+; B1a cells, CD19+ CD45R- IgM^{hi} CD5+; B1b cells, CD19+ CD45R- IgM^{hi} CD5-.)

Discussion & Conclusion

As there was no significant changes in the population of intrahepatic B cells in STAP1 KO mice upon NAFLD, the cytokines secretion profile of intrahepatic B cells and cell compositions of other immune cells will be explored. In summary, our finding provides a potential novel function of STAP1 in the progression of DIO-induced NAFLD. (The study is supported by HMRF 04152366.)